lated optimum is employed for signal acquisition. In one embodiment of the invention, the pseudo random sequence range extends from 1-bit extended pseudo random sequence (1 ion packet release per IMS separation) to 7-bit extended pseudo-random sequence (64 ion packet releases per IMS separation). Once the optimum sequence has been selected, the instrument then controls the gates of entry to the drift tube according to the preselected protocol. The optimum sequence is repeated for a number of pre-determined averages for signal acquisition and the instrument control system is then reset back to the pre-scan mode. In as much as this process can be repeatedly performed, this allows for increased efficiency in obtaining desired results.

[0011] The proposed design for the dynamic multiplexed IMS-TOF platform coupled to an automated LC fraction collection instrument will enable a complete 3D sample analysis in <10 min at an IMS duty cycle of >50% and a mass accuracy of <5 ppm. This approach will result in automated analysis of >100 technical replicate analyses per day. In addition, the same approach will provide high sensitivity fragmentation data and complete sequence information for biologically regulated species. The purpose of the foregoing abstract is to enable the United States Patent and Trademark Office and the public generally, especially the scientists, engineers, and practitioners in the art who are not familiar with patent or legal terms or phraseology, to determine quickly from a cursory inspection the nature and essence of the technical disclosure of the application. The abstract is neither intended to define the invention of the application, which is measured by the claims, nor is it intended to be limiting as to the scope of the invention in any way.

[0012] Various advantages and novel features of the present invention are described herein and will become further readily apparent to those skilled in this art from the following detailed description. In the preceding and following descriptions, we have shown and described only the preferred embodiment of the invention, by way of illustration of the best mode contemplated for carrying out the invention. As will be realized, the invention is capable of modification in various respects without departing from the invention. Accordingly, the drawings and description of the preferred embodiment set forth hereafter are to be regarded as illustrative in nature, and not as restrictive.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] FIG. **1** shows the schematic of an IMS-TOFMS instrument used in dynamic multiplexing experiments.

[0014] FIG. **2** shows the modulation waveforms that were applied to the ion trap end-cap electrodes (i.e., grids) to introduce ions into the accumulation region of the ion trap, block ions from the continuous ion source and extract accumulated ion packets from the ion trap into the IMS drift tube

[0015] FIG. **3** shows the flow control diagram of the dynamic multiplexing experiment

[0016] FIG. **4** shows two dimensional contours along with IMS and mass spectra of the encoded and reconstructed peptide signals from depleted human plasma sample obtained under the present method. A) Signal from fraction **14** using 5 bit encoding sequence; B) Reconstructed signal from data in A); C) Signal from fraction **7** using signal averaging acquisition.

[0017] FIG. **5** shows a signal that was encoded with 5-bit extended pseudo-random sequence described in the present invention.

[0018] FIG. **6** shows an extracted ion chromatogram corresponding to the IMS-TOF signal in FIG. **2**.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0019] The following description includes a preferred best mode of one embodiment of the present invention. It will be clear from this description of the invention that the invention is not limited to these illustrated embodiments but that the invention also includes a variety of modifications and embodiments thereto. Therefore the present description should be seen as illustrative and not limiting. While the invention is susceptible of various modifications and alternative constructions, it should be understood, that there is no intention to limit the invention to the specific form disclosed, but, on the contrary, the invention is to cover all modifications, alternative constructions, and equivalents falling within the spirit and scope of the invention as defined in the claims.

[0020] As has been discussed previously, a multiplexed IMS-TOF approach has been shown to provide up to 10-fold increase in sensitivity as compared to the conventional signal averaging approach in regard to analysis of peptide mixtures. This sensitivity improvement is based on introduction of multiple ion packets into an IMS drift tube on the time scale of a single measurement in the signal averaging experiment. Each ion packet injection occurs during a constant IMS gate open event, and the ion injection process is governed by an extended pseudo-random sequence that mitigates diffusion-driven ion cloud expansion and enables efficient ion accumulation prior to each gate open event. Short (~100 us) IMS gate open events minimize contribution of the ion injection term on IMS resolving power.

[0021] The need in multiplexing the IMS-TOF is strongly dictated by the total number of analytes molecules delivered to the ion trap (preceding the IMS drift tube) per unit time and by the charge capacity of that trap. Given lower abundance signals, ion trap may remain under filled with ions in the course of IMS separation, implying no need in multiplexing to attain efficient ion utilization. In this case, ion accumulation over the entire IMS separation would rather be beneficial for achieving high sensitivity. One the other hand, if accumulated on the timescale of IMS separation, higher abundance ion species may result in the over filling of the ion trap, implying the need for multiple ion releases from the trap per single IMS separation to achieve high sensitivity and dynamic range. In addition, the over filling of the ion trap may result in a number of undesired effects, including ion discrimination and fragmentation. Therefore, a combination of approaches is needed to maximize instrument sensitivity in analysis of complex samples with broad dynamic range.

[0022] In one embodiment, the present invention is employed with fully automated fast sample fractionation, using either strong cation/anion exchange (SCX/SAX), reverse phase (RP) capillary liquid chromatography (LC) or capillary electrophoresis (CE) separations. LC/CE separation timescale determines the analysis time. Analysis of each fraction is accomplished in two steps, first an initial short IMS-TOF pre-scan is employed to determine the experimental sequence. Secondly, a longer full IMS-TOF scan to acquire data takes place. Each IMS-TOF pre-scan is typically be conducted in the signal averaging mode using constant short accumulation times (<1 ms) to ensure that operation of the ion trap in the linear dynamic range for higher concentration fractions takes place. Following several 60-ms long IMS-